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Cerebral Blood Flow Responses to Aquatic Treadmill Exercise

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Cerebral blood flow and aquatic exercise

Abstract

Introduction. Aquatic treadmills are used as a rehabilitation method for conditions such as spinal cord injury, osteoarthritis and stroke, and can facilitate an earlier return to exercise training for athletes. However, their effect on cerebral blood flow (CBF) responses has not been examined. We tested the hypothesis that aquatic treadmill exercise would augment CBF and lower heart rate compared to land-based treadmill exercise.

Methods: Eleven participants completed incremental exercise (crossover design) starting from walking pace [4 km/h, immersed to iliac crest (aquatic), 6 km/h (land)] and increasing 1 km/h every 2 min up to 10 km/h for aquatic (maximum belt speed) or 12 km/h for land. Following this, participants completed two 2-min bouts of exercise immersed to mid-thigh and mid-chest at constant submaximal speed (aquatic), or were ramped to exhaustion (land; increased gradient 2° every min). Middle cerebral flow velocity (MCAv) and heart rate (HR) were measured throughout, and the initial 10 min of each protocol and responses at each immersion level were compared.

Results. Compared to land-based treadmill, $MCAv_{mean}$ increased more from baseline for aquatic exercise (21 vs. 12%; $p<0.001$), while being associated with lower overall HR (pooled difference: 11 b/min; $p<0.001$). $MCAv_{mean}$ increased similarly during aquatic walking compared to land-based moderate intensity running (~10 cm/s; $p=0.56$). Greater water immersion lowered HR (139 vs. 178 b/min for mid-chest vs. mid-thigh), while $MCAv_{mean}$ remained constant ($P=0.37$).

Conclusion. Findings illustrate the potential for aquatic treadmill exercise to enhance exercise-induced elevations in CBF, and thus optimise shear-stress mediated adaptation of the cerebrovasculature.

Key words: Cerebral blood flow, Aquatic treadmill exercise, Deep-water running, neurorehabilitation, brain health

INTRODUCTION

Aquatic treadmill (ATM) exercise allows for lower impact and increased resistance in comparison to land-based treadmill (LTM) exercise, therefore achieving decreased musculoskeletal loading of joints and providing potential for enhanced acute and chronic physiological adaptations (5). The increased hydrostatic pressure applied to the human body upon immersion in water leads to centralising blood distribution within the body, which enhances cardiac performance and therefore increases tissue perfusion (32). Furthermore, the mechanical unloading and support of bodyweight due to buoyancy means that ATMs are a useful tool in gait re-education. Indeed, ATM exercise is utilised in the rehabilitation of spinal cord injuries (36) and stroke (28) patients. Positive effects of ATM exercise have also been noted in populations with joint conditions such as osteoarthritis (7), and those with coronary heart disease (13). At the other end of the spectrum, athletes utilise ATM exercise to maintain cardiorespiratory fitness while reducing the mechanical load when recovering from injury (30). Therefore, ATM exercise represents an effective form of therapy and rehabilitation for a range of healthy and diseased populations. Studies to date comparing physiological responses between aquatic- and land-based treadmills have mostly focused on cardiorespiratory responses (e.g., (17, 35); while no study has examined the effect that ATM exercise has on cerebrovascular responses, and therefore explored the possibility of how this mode of therapy may optimise exercise-induced, stimulus-response adaptations leading to improved cerebrovascular function and ultimately brain health (11).

Effective regulation of blood flow to and within the brain is vital for optimal brain function. Regular exercise and higher cardiorespiratory fitness has been positively linked with CBF and its regulation (e.g., (3, 6)), shown to offset the natural age-related decline in CBF (1), and reduce risk of neurodegenerative disease (e.g., dementia (21)). However, the mechanisms that underpin the neuroprotective benefits of exercise are yet to be established, meaning that the effectiveness of various exercise parameters such as mode, intensity and duration are not yet understood (22). One

suggested mechanism for exercise-induced improvements in vascular function is via shear-stress mediated increases in endothelium nitric oxide-dependent vasodilation of blood vessels (18, 39), as a consequence of the recurrent mechanical force of blood flow on the walls of the arteries (i.e. shear stress) (27). Numerous studies [e.g., (9, 15, 19)] have reported the functional adaptation and structural changes to the vasculature that occur as a result of long-term exercise (18), albeit primarily provided from animal-based and cell-culture studies [see (8)] or within the peripheral vasculature of humans. Researchers have begun to explore alternative methods [e.g. heat therapy (12, 38)] that target this mechanism to improve vascular function. Extrapolating this to the brain, conditioning strategies that increase blood flow, either in combination or independent of exercise, may enhance shear-stress mediated adaptation of the cerebrovasculature. This has the potential to directly improve CBF and its regulation and therefore be used in the prevention and treatment of neurovascular disease.

Given the known physiological responses to water immersion, water-based activities may be one such strategy. Indeed, two studies have explored this possibility, examining CBF responses in water at rest (12) and during a box-stepping exercise protocol (31). Carter et al. (12) reported a positive correlation between middle and posterior CBF velocities during resting water immersion, linking the increase in CBF velocity during immersion to an increase in mean arterial pressure and arterial carbon dioxide content. From the same group, Pugh et al. (31) compared a 20-min bout of matched low-intensity stepping exercise (HR $\leq$ 100 b·min^{-1}) in a water tank to that on land, finding CBF velocities to be augmented in water. These studies illustrate the potential for enhanced shear-stress mediated vascular adaptation by exercising in water, although important questions remain unanswered relating to the CBF profile during different exercise intensities and at different depths of water immersion. Such questions can be addressed using an aquatic treadmill, which is already an established rehabilitation tool for a number of conditions (see above). Therefore, the primary purpose of this study was to compare changes in CBF (velocity) and heart rate responses during an incremental exercise test using an aquatic treadmill and a land-based treadmill, and to examine CBF

and heart rate responses at different levels of immersion (mid-thigh, iliac crest (hip) and xiphoid process (mid-chest)) during aquatic treadmill exercise. We hypothesised that: 1) aquatic treadmill exercise would augment the CBF response to an incremental intensity exercise test compared to land-based treadmill exercise, and 2) increased water immersion would maintain CBF while lowering heart rate.

METHODS

Participants

Eleven healthy participants (7 females and 4 males; aged 27 ± 5 years) were recruited for this study, which was approved by the University of Birmingham Science, Technology, Engineering and Mathematics Ethical Review Committee, and performed in accordance with the *Declaration of Helsinki*. After providing their written informed consent, all participants completed a General Health Questionnaire during an initial visit to the laboratory and declared that they were free of any cardiovascular, cerebrovascular or respiratory disease, were not taking medication (not including contraceptive medications), or had injuries that would preclude treadmill-based exercise.

Study Design and Protocol

Following the initial screening visit, participants completed exercise sessions on both a land-based (LTM) and an aquatic treadmill (ATM) in a randomised, counterbalanced order. Each session lasted approximately 1 hour, of which 15-25 minutes were exercise. First, participants completed incremental exercise starting from walking pace [4 $km \cdot h^{-1}$, immersed to iliac crest (aquatic), 6 $km \cdot h^{-1}$ (land)] and increasing 1 $km \cdot h^{-1}$ every 2 min up to 10 $km \cdot h^{-1}$ for aquatic (maximum belt speed) or 12 $km \cdot h^{-1}$ for land. On land, participants were then ramped to exhaustion (increased gradient 2° every min), whereas for aquatic exercise participants completed two 2-min bouts of exercise immersed to mid-thigh and mid-chest at constant submaximal speed. During exercise at the different immersion depths on the ATM the speed was held constant; eight participants completed this protocol at 10 $km \cdot h^{-1}$, while for 3 participants, who reached near maximal heart rate during the

initial incremental intensity protocol, the treadmill speed was lowered (to 8 $km \cdot h^{-1}$ for 2 participants and 5 $km \cdot h^{-1}$ for 1 participant) and remained at this speed during the exercise at different immersion depths. Figure 1 provides a schematic for the ATM and LTM protocols.

There were at least 48 hours between sessions for each participant, with the majority of participants completing their second session within 2 weeks of the first. Due to the timing of access to the ATM facility, the phase of menstrual cycle for female participants was not controlled for between exercise sessions. Prior to each session participants were asked to refrain from eating a large meal for 4 hours before arrival, although a light meal was permitted up to 2 hours before arrival. In order to ensure adequate hydration status, participants were advised to drink 0.5 litres of water within 4 hours of beginning testing and 0.25 litres of water within 15 minutes of testing, in accordance with the American College of Sports Medicine Hydration Guidelines (2). Participants were also asked to refrain from caffeine for 6 hours prior to testing, and refrain from vigorous exercise and the consumption of alcohol for 24 hours prior to testing.

Equipment and Measurements

Exercise treadmills: A standard treadmill ergometer (Pulsar, H-P-Cosmos, Germany) was used for the land-based exercise protocol. The aquatic exercise session was completed on an aquatic treadmill (FOCUS, HYDRO PHYSIO^{TM}, UK) at the Optispine Physiotherapy Clinic in Birmingham.

Cerebral blood flow velocity (CBFv) and heart rate measures: Bilateral blood flow velocity in the left and right middle cerebral arteries (MCAv) was measured using a 2-MHz transcranial Doppler (TCD) ultrasound system (Dopplerbox, DWL, Compumedics LTD, Germany), in accordance with search techniques described elsewhere (40). The two ultrasound probes were placed above each zygomatic arch on the left and right side of the head and secured via an adjustable headband that maintained a constant insonation angle throughout the testing session. A small amount of ultrasound gel was placed between the probe and the skin to obtain the highest quality images. The reliability of measuring CBF using TCD is operator-dependant, thus all

measurements were taken by the same experienced sonographer (SJEL), with photographs of probe placement, and depth and filter settings recorded and kept constant between exercise sessions for each participant. Cerebrovascular data were acquired continuously via an analogue-to-digital converter (PowerLab 8/30, ML870, ADInstruments, Dunedin, New Zealand) at 1KHz. Data were displayed in real time and recorded for off-line analysis using commercially available LabChart Pro software (v7, ADInstruments).

Heart rate (HR) was monitored using telemetry (Polar, Finland) via a belt fitted around the chest of the participant, as well as derived from the beat-by-beat MCAv waveform. Steady-state measures for HR were recorded at each stage of the incremental protocols and for the different immersion depths.

Data analysis and statistical approach

Mean values for MCAv and HR at each 2-min stage were determined using an average of the final 30 seconds of each stage, and used to calculate change from resting (seated) baseline for each measured time point. Since the aquatic treadmill had a maximum speed of 10 $km \cdot h^{-1}$, we intended to use the initial 14 minutes of each protocol to compare the responses between the aquatic and land treadmill exercise. We also independently compared two exercise intensities; specifically, walking and the recommended public health guideline of moderate exercise intensity (65% $\dot{V}O_2max$), which was from estimated from heart rate measures. Walking pace in the aquatic treadmill was 4 $km \cdot h^{-1}$, whereas on the land treadmill it was 6 $km \cdot h^{-1}$, but both represented the only speed for which all participants were walking; i.e., participants started jogging in the ATM at 5 $km \cdot h^{-1}$. The 65% $\dot{V}O_2max$ intensity was estimated at 79% HRmax (37), and treadmill speeds that induced a heart rate response closet to this target were selected (range for land: 7 - 11 $km \cdot h^{-1}$, range for aquatic: 5 - 10 $km \cdot h^{-1}$).

Two-way repeated measures ANOVA were used to compare changes in $MCAv_{mean}$ and HR across the incremental protocol (time * treadmill) and at walking and 65% $\dot{V}O_2max$ intensity

(intensity * treadmill), while a one-way ANOVA compared changes in $MCAv_{mean}$ and HR across the three different immersion levels while running at the same speed in the aquatic treadmill. Post-hoc comparisons were done using pairwise comparisons (Bonferroni corrected) to show where effects occurred. Paired t-tests were used to determine whether significant differences existed between comparable data sets of interest (e.g., resting and peak HR/MCAv, MCAv during walking vs. 65% $\dot{V}O_2max$). All statistical analysis was carried out using SPSS statistical software (v22, Chicago, USA), with *a priori* statistical significance set at $P \leq 0.05$. Data are presented as mean ± SD.

RESULTS

All 11 participants who began the exercise sessions completed both protocols. All eleven participants reached the maximum belt speed in the aquatic treadmill (10 $km \cdot h^{-1}$), therefore completing all 14 min of incremental aquatic exercise. For the land-based treadmill protocol, one participant stopped at the completion of the 10 $km \cdot h^{-1}$ stage (at 10 min) and two participants stopped after the 11 $km \cdot h^{-1}$ stage (at 12 min) due to reaching voluntary exhaustion. Consequentially, the two-way ANOVA for the comparison of incremental exercise protocols used the first 5 stages of exercise for which all 11 participants had paired data sets for (as indicated in Figure 1).

There was no significant difference (P=0.79) between left and right $MCAv_{mean}$ in participants that had a TCD signal on both sides throughout testing in both sessions (n=6), therefore data were pooled and presented as a combined mean value. In 4 aquatic sessions and one land-based session, the TCD signal on one side was either lost during exercise or not found initially; for these trials the remaining side was used as the mean value.

There was a small, but significant, difference for baseline resting (seated) $MCAv_{mean}$ between land and aquatic testing sessions (70 ± 9 $cm \cdot s^{-1}$ vs. 66 ± 9 $cm \cdot s^{-1}$, respectively; p=0.023), while resting HR was similar (70 ± 13 $b \cdot min^{-1}$ vs. 69 ± 14 $b \cdot min^{-1}$; p=0.738).

Effects of increased exercise intensity on cerebrovascular and heart rate responses

As illustrated in Figure 2A, there was a significant main effect of time (p=0.004) and treadmill type (p=0.003) on the change in $MCAv_{mean}$ from baseline over the initial 10 minutes of each protocol. The pooled difference across the 10 minutes for $MCAv_{mean}$ between the treadmill protocols was ~6 $cm \cdot s^{-1}$, with the largest difference occurring at the 4-min stage (~11 $cm \cdot s^{-1}$). The 4-min stage also represented the peak change in $MCAv_{mean}$ from baseline in the water (~16 $cm \cdot s^{-1}$), which was maintained to within 3 $cm \cdot s^{-1}$ for the remainder of the protocol. On land, however, the peak change in $MCAv_{mean}$ (~12 $cm \cdot s^{-1}$) did not occur until the 10^{th} minute. Nevertheless, this difference in the pattern of increase did not reach statistical significance (interaction effect: p=0.073).

For HR, there was an interaction effect for the change in HR across time (p=0.020). Post-hoc analysis revealed that HR increased for each incremental stage except for the transition between 5 and 6 $km \cdot h^{-1}$ (mins 4 and 6) on the ATM, and HR was significantly higher on the LTM than the ATM except for at 4 minutes (7 and 5 $km \cdot h^{-1}$, respectively, see Figure 2B). Overall, and in contrast to the $MCAv_{mean}$ observations, HR was higher with land-based exercise compared to aquatic exercise (pooled difference: ~11 $b \cdot min^{-1}$ greater for land; main effect: p=0.028). Further, the peak $MCAv_{mean}$ during the aquatic incremental protocol tended to be at a lower percentage of HR_{max} (determined during the land-based protocol) compared to land-based incremental exercise (75 ± 12% vs. 84 ± 15% of HR_{max} for aquatic and land, respectively; p=0.069).

Figure 3 shows the comparison between walking and moderate intensity running (at 65% $\dot{V}O_2max$) on each treadmill for $MCAv_{mean}$ and HR responses. Both walking and running at 65% $\dot{V}O_2max$ elicited a greater increase in $MCAv_{mean}$ during ATM as compared to LTM (main effect: p=0.003). Interestingly, while there was a main effect of intensity (p=0.022) for $MCAv_{mean}$, subsequent analysis revealed that while $MCAv_{mean}$ increased similarly within each treadmill modality (interaction effect: p=0.628), there was no difference between $MCAv_{mean}$ for ATM walking and LTM running at 65% $\dot{V}O_2max$ (paired ttest: p=0.563).

Collectively, these data indicate that water-based exercise across a range of intensities stimulates greater increases in MCAv for a relatively lower heart rate response compared to land-based exercise, and that water-based walking elicits a similar increase in blood flow (velocity) as running on land at 65% $\dot{V}O_2$max.

Effect of immersion level on cerebrovascular and heart rate responses

Figure 4 illustrates that HR decreased with greater levels of water immersion on the aquatic treadmill while the treadmill belt speed remained constant. Post-hoc analysis showed that the mean decrease in HR from the water level at mid-thigh to iliac crest was ~18 b·min^{-1} ($p=0.001$), and from iliac crest to xiphoid process was ~21 b·min^{-1} ($p=0.002$). This was in contrast to $MCAv_{mean}$, with the change from resting baseline not different between immersion levels ($p=0.371$). Finally, the 2-min exercise bout at mid-thigh water depth elicited near maximal heart rates (95 ± 5% of HR_{max}; see figure 4).

DISCUSSION

The aim of this study was to examine CBF responses during incremental exercise on an aquatic treadmill as compared to a land-based treadmill, and while exercising at different levels of water immersion on the aquatic treadmill. Our main novel findings were that: 1) $MCAv_{mean}$ was augmented during aquatic treadmill exercise compared to land-based treadmill exercise across the range of exercise intensities tested, and this augmented $MCAv_{mean}$ was associated with a relatively lower heart rate response; 2) walking on an aquatic treadmill elicited a similar increase in $MCAv_{mean}$ to that of running at moderate intensity (65% $\dot{V}O_2$max) on land, and 3) immersion depth altered heart rate while maintaining $MCAv_{mean}$ during exercise at a constant aquatic treadmill speed. Collectively, these data indicate that aquatic treadmill exercise augments CBF. Further, although we

have not quantified differences in shear stress *per se*, the elevated flow velocity demonstrates the potential for aquatic treadmill exercise to enhance shear-stress mediated cerebrovascular adaptation and thus optimise exercise-induced adaptations linked with improved brain health.

The findings of the current study are consistent with previous research reporting elevated MCAv during exercise (e.g., (10, 23), and an augmented MCAv response when in water [observed at rest and during light intensity exercise (12, 31)]. Here, we show for the first time that this augmented MCAv response occurs across a range of exercise intensities and that MCAv can be maintained while exercising at lower intensities with greater depths of water immersion. One notable observation was that walking on an aquatic treadmill elicited a similar increase in MCAv (~10 $cm \cdot s^{-1}$) to that of running on land at the exercise intensity promoted by current public health guidelines (i.e., 65% of aerobic capacity for 150 min / week). Furthermore, the profile of exercise-induced changes in MCAv was different between the protocols, with ATM exercise producing maximal gains in MCAv within 4 minutes of starting the protocol, a time point that also represented the greatest difference between treadmill protocols, while MCAv during LTM exercise increased linearly across the incremental protocol yet remained lower (see Figure 2).

It is widely reported that the greatest exercise-induced elevation in CBF is achieved at moderate exercise intensity (~65% $\dot{V}O_2max$), as above this threshold CBF will decrease back towards resting values as a result of hyperventilation-induced cerebral vasoconstriction due to lower $PaCO_2$ (24). Our data indicate that aquatic treadmill exercise may have a different exercise-induced CBF profile to this commonly reported profile, most of which come from cycling-based exercise protocols. The findings of the current study indicate that optimal CBF gains may be achieved at lower exercise intensities in water than on land (see Figure 2A), and even at higher exercise intensities (induced via less water immersion) MCAv is consistently elevated above resting measures (see Figure 4). Based on these findings it could be suggested that changes in arterial carbon dioxide above anaerobic threshold during aquatic treadmill exercise has less influence on CBF relative to other factors involved in CBF regulation (e.g., blood pressure, cardiac output).

Unfortunately, we were unable to measure end-tidal PCO_2 during our study due to equipment unavailability, thus we can only speculate about the relation between PCO_2 and CBF during aquatic treadmill exercise. Further research is needed in order to determine the influence of this key regulator of CBF during aquatic treadmill exercise of increasing exercise intensity.

The regulation of CBF during exercise is multifactorial and complex (25), with an integrative combination of exercise-induced changes in brain metabolic and neuronal activity, blood pressure, cardiac output and arterial PCO_2 all likely to contribute to changes in cerebral perfusion during any exercise paradigm. Based on previous water immersion studies (12, 31), an elevated PCO_2 likely explains some of the difference in $MCAv_{mean}$ with aquatic exercise as compared to land-based exercise. Further, given the linear relation between cardiac output and CBF (26), another likely contributor to the augmented blood flow velocity is related to the well-documented increases in cardiac output during water immersion (29), due to the effects of increased hydrostatic pressure centralising blood within the trunk and increasing stroke volume (5). Interestingly, an elevated stroke volume would appear to be the key mediator of this increased cardiac output, since a reduction in HR (as we observed) during water immersion is also well documented (4, 16, 20). In contrast, Pugh et al. (31) reported no significant difference in HR between water and land during their low-intensity exercise. However, it is worth noting that the box-stepping exercises in their study were matched for HR between land and water protocols in order to compare similar intensities. Importantly, regardless of the mechanisms regulating CBF during this modality of exercise, our observed differences in exercising MCAv between our treadmill protocols demonstrates that aquatic treadmill exercise produces higher blood flow velocity across a range of intensities, and particularly so at lower exercise intensities (i.e., walking / light jogging); thus illustrating the potential for an enhanced shear-stress mediated pathway for cerebrovascular adaptation following repeated exposure (i.e., training).

The decrease in HR associated with increasing immersion levels noted in this study is supported by previous studies that have reported a continuous decrease in HR from hip level up to

head-out immersion in water at rest (4, 20). Our findings illustrate that a similar elevation in $MCAv_{mean}$ can be achieved with greater water immersion for a comparatively lower heart rate. As such, aquatic treadmill exercise training at higher levels of water immersion could optimise shear-stress mediated vasculature adaptations, while lowering the risk of a cardiac event in populations with elevated risk.

The water temperature used in this study (32^0C) is representative of conditions regularly used in rehabilitative therapy, and is within 3^0C of the temperatures used in previous studies. While changes in water temperature have been reported to translate into changes in the cardiac response (5), the relatively small variation ($<2^0$C) in temperature between this study and recent research (12, 31) is unlikely to impact on the relative changes in $MCAv_{mean}$ and HR observed here. Another consideration is the different heat conduction capacities of water versus air, which may differentially alter exercise-induced changes in body core temperature. As such, measures of body core temperature would be of value in future studies to assess differences between modalities and potential effects of thermal stress related adaptations during the aquatic treadmill exercise. Indeed, one further possibility for this form of exercise therapy is to alter the water temperature to investigate the potential additive therapeutic impact of thermal stress, which may further optimise the stimulus-response interaction and promote greater neuroprotection against neurodegenerative diseases (11).

Limitations

Speed limitations of the aquatic treadmill prevented a full comparison between treadmill modalities for an incremental test to exhaustion. Nevertheless, both protocols started at a walking pace and increased at the same rate (1 $km \cdot h^{-1}$ every 2 minutes), which resulted in a similar rate of increase in HR and therefore allowed for a meaningful comparison between the aquatic- and land-based treadmill exercise across a range of exercise intensities. This study design meant we were unable to compare matched HR responses across all intensities. We acknowledge that the differences in cardiorespiratory responses may influence the absolute values we show here, but

ultimately will not affect the pattern of MCAv that we observed across the range of exercise intensities we tested. Measurements of $\dot{V}O_2$ were originally planned in addition to HR to further quantify the cardiorespiratory strain and energy expenditure during both protocols, but this was not possible due to equipment unavailability. However, similar decreases in HR and $\dot{V}O_2$ between land running and deep and shallow water running have previously been noted (16), indicating that heart rate alone can adequately reflect measures of exercise intensity on land as compared to in water. It is also acknowledged that the reduction in heart rate alone does not necessarily reflect a reduction in cardiac work (as reflected by myocardial $\dot{V}O_2$). Given the linear relationship that $\dot{V}O_2$ and cardiac output share (14), cardiac work can be indexed via the combined measures of heart rate, stroke volume and blood pressure (i.e., HR x SV x systolic BP (or MAP); (33)) . However, we chose not to fit a blood pressure measuring device (e.g., finometer) so that participants could perform the exercise in the water as naturally as possible (i.e., fitting this device would have required them to hold their arm up out of the water). In addition to providing a measure of stroke volume (e.g., via Beatscope software) to determine cardiac work, measures of BP would have also provided insightful data regarding the influence of blood pressure on CBF for these different exercise modalities. Nevertheless, our primary question was to examine the CBF (velocity) differences between these modalities across a range of exercise intensities and at different immersion depths. The mechanism(s) that underpin these differences were not the primary focus of our study, but based on previous studies (12, 32), differences in BP (and $P_{ET}CO_2$) would likely be involved.

As mentioned above, we were also unable to measure end-tidal gas content and therefore assess the influence of $P_{ET}CO_2$ on MCAv during our exercise protocols. Nevertheless, given the earlier peak in $MCAv_{mean}$ during the initial incremental protocol on the aquatic treadmill and the consistently elevated $MCAv_{mean}$ during near maximal exercise in water (see Figures 2 and 4), the typical influence of changes in $PaCO_2$ on CBF during exercise would appear to be different for aquatic treadmill exercise. Future studies that include measures of both $\dot{V}O_2$ and $P_{ET}CO_2$ are needed

306 to confirm the hypothesis that there may be an altered relation between CBF and PCO_2 during
307 aquatic treadmill exercise.

308 We measured blood flow velocity using transcranial Doppler as an index of CBF. The
309 validity of this approach and the likelihood of vessel diameter changes affecting interpretations of
310 these measures should be considered, especially given the likely changes in blood pressure and
311 PCO_2 associated with exercise. Nevertheless, given the differential pattern of MCAv changes
312 between the ATM and LTM protocols while changes in $P_{ET}CO_2$ and BP were likely similar [albeit
313 elevated in water (12, 31)], it seems unlikely that changes in MCA diameter would affect the
314 interpretation of the findings here. Further, TCD is the ideal brain imaging tool to use in this setting,
315 while other approaches are not feasible or realistic (e.g., MRI or Duplex Doppler).

316 Finally, the relatively small and demographically limited sample population (mostly young
317 university students) should be taken into account. As such, whether similar responses occur in older
318 and clinical populations remain to be determined.

319 *Implications*

320 Based on the findings of the current study, aquatic-based treadmill exercise could provide an
321 ideal exercise modality to maximise the stimulus-response for shear-stress mediated adaptation of
322 the cerebrovasculature in clinical and non-clinical populations. Research is now needed to establish
323 whether this augmented acute response translates into permanent adaptation of the
324 cerebrovasculature, and how such training may improve other aspects of brain structure and
325 function.

326 Exercise training is recommended in clinical populations with elevated risk of
327 neurodegenerative disease to aid rehabilitation (e.g., stroke (34)), however physical disability may
328 impact on the effectiveness of traditional exercise programmes to improve vascular health via
329 shear-stress mediated adaptation. Our findings demonstrate the potential for aquatic treadmill
330 exercise to optimise this stimulus for vascular adaptation at exercise intensities (e.g., walking) that

are feasible for clinical populations with impaired physical function (e.g., stroke survivors). As such, the utility of aquatic treadmills for brain-targeted exercise training may be another important reason to promote such a rehabilitation approach.

Conclusion

Aquatic treadmill exercise augments cerebral blood flow velocity across a range of intensities, and particularly so at lower exercise intensities (i.e., walking / light jogging). This elevated blood flow has the potential to enhance shear-stress mediated cerebrovascular adaptation and thus optimise exercise-induced adaptations linked with improved brain health. Research is now needed to establish whether this augmented acute response translates into permanent adaptation of the cerebrovasculature, and how such training may improve other aspects of brain structure and function.

AUTHOR CONTRIBUTIONS

RP, MH, SJEL were involved in conception and design of research. RP and SJEL conducted experiment, performed data analysis and interpretation, and contributed to the drafting the manuscript. MH provided critical review of the manuscript. All authors approved the final version of this manuscript.

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manipulation. We also acknowledge that the results of the present study do not constitute endorsement by ACSM.

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Disclosure

There were no conflicts of interest

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457

458 **Figure 1:** Schematic outlining treadmill belt speed, land treadmill gradient and aquatic treadmill
459 water depth for the aquatic- and land-based treadmill exercise protocols. Participants completed
460 seven 2-min stages of incremental exercise intensity, induced via 1 $km \cdot h^{-1}$ increases in treadmill belt
461 speed. Participants were then ramped to exhaustion (2° every minute) for the land-based protocol or
462 completed two 2-min stages of exercise at two alterative water depths on the aquatic treadmill.
463 Numbers of participants completing each stage of the land-based protocol through to exhaustion are
464 shown, along with the numbers of participants at each submaximal aquatic belt speed for the 2-min
465 stages of different immersion depths. Room temperature was maintained at ~21^0C for both, while
466 water temperature was 32^0C. Abbreviations: ATM, aquatic treadmill; LTM, land-based treadmill.

467

468 **Figure 2:** Changes in middle cerebral artery blood flow velocity ($MCAv_{mean,}$ A) and heart rate (B)
469 from resting (seated) baseline values over the initial 10 minutes of aquatic- and land-based exercise
470 protocols. Data are means ± SD. Symbols: * significant difference between treadmills; # significant
471 difference between preceding stage.

472

473 **Figure 3:** Mean change in $MCAv_{mean}$ (left panel) and HR (right panel) from resting baseline for
474 walking and moderate intensity (65% VO_2max) running exercise using land- and aquatic-based
475 treadmills. Data are means ±SD. N=11. * significant difference between treadmills; # significant
476 difference between preceding stage.

477

478 **Figure 4:** Changes in middle cerebral blood flow velocity ($MCAv_{mean}$) and heart rate from resting
479 (seated) baseline values during constant speed aquatic treadmill exercise immersed to mid-thigh,
480 iliac crest and xiphoid process. Data are means ±SD for 11 participants. * different from mid-thigh
481 ($p<0.05$); † different from iliac crest ($p<0.05$).